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(54) Title: ELECTROCHEMICAL BIOSENSORS

(57) Abstract

An electrochemical biosensor for determining the level of a target chemical in a biological fluid includes an electrochemical system including an enzyme substrate which reacts with the target chemical to yield a system signal related to the concentration in the biological fluid of said target chemical. The biosensor includes a first membrane for immobilizing the enzyme substrate. The first membrane has a porosity permitting passage therethrough of the target chemical to react with the enzyme substrate and a surface exposed to the biological fluid characterized by electron donor site susceptible to facilitating attachment thereon of proteins and fibrin which impair the system signal. A second membrane is bonded to the electron donor sites of the first membrane. The second membrane is formed of a phenyl based polymer having connecting hydrogen atom donors which bond to the hydrogen atom donors bonding to the electron donor sites at least sufficiently to form an outer surface on the first membrane exposed to the biological fluid consisting of phenyl rings without significantly changing the porosity provided by the first membrane.

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ELECTROCHEMICAL BIOSENSORS

FIELD OF THE INVENTION

The present invention relates to means for detecting a broad range of chemicals and biological substances that may be found in blood or other physiological fluids including electrochemical biosensors for determining the levels of chemicals in biological fluids, and in particular, an implantable glucose sensor for determining in vivo the concentration of blood glucose levels.

BACKGROUND OF THE INVENTION

Electrochemical biosensors are used, both in vitro and in vivo, to determine the levels of chemicals in biological fluids. For example, blood glucose sensors are used to determine the concentration of glucose in blood sera. Oxygen sensors are used to measure oxygen levels in blood. Other examples are potassium, calcium, pH, CO_2, sodium, chloride sensors and the like. Such sensors use an enzyme, immobilized by a membrane sheathing, coupled to an electrochemical system. The target chemical in the biological fluid reacts with the enzyme to generate a current signal related to the target chemical concentration, which signal is processed by the system to provide an output indicative thereof.

While well defined for in vitro testing and used routinely therefor, there has been a long-felt need in the art for implantable or indwelling biosensors that can function, reliably without drift or recalibrating caused by biological overgrowth and attachment, for extended times in recipient patients. Implantable glucose sensors were first proposed in the 1960's (Gough et al., Diabetes, Vol. 44, pp.190-198). However, to date no successful biosensor has been developed notwithstanding advances which have yielded

successful in vitro versions which function for somewhat extended periods but are prone to biological overgrowth and fouling. Such biosensors are well characterized in the art and generally fall into the categories of hydrogen peroxide-based enzyme electrode sensors, oxygen-based enzyme electrode sensors, mediator-based enzyme electrode sensors, membrane covered catalytic electrodes and others.

The most significant reason for an inability to function reliably long-term in vivo appears to be biological fouling of the electrode membrane resulting in a progressive reduction in sensing area and resultant drift in electrical signal, ultimately leading to complete blockage of the membrane and the loss of meaningful signal. These membranes currently function adequately in most regards. Examples of such membranes include polyurethane, cellulose acetate, perfluorosulfonic acid polymer (Nafion®), and other like membrane materials. Such membranes are considered biocompatible in the sense that they do not elicit an inflammatory response in the host. However, these membrane materials have reactive groups which provide attachment sites for biological overgrowth leading to the membrane fouling discussed above.

It would thus be desirable to provide an electrochemical biosensor based on current and future designs while protecting the membrane from performance-degrading biological overgrowth.

SUMMARY OF THE INVENTION

The present invention achieves the above and other significant objectives and provides an improved electrochemical biosensor that limits biological overgrowth and attachment to the membrane and permits extended indwelling determination of target biological chemicals. This is achieved by passivating the biological active sites on the membrane without

significantly affecting the functional properties of the membrane, i.e., porosity and diffusion. This is achieved by applying a second membrane over the first membrane, the second membrane being characterized by a phenyl-based polymer having connecting hydrogen donors bonded to the biologically active sites on the first polymer without significantly affecting the properties of the first membrane. Preferably, the polymer is selected from the parylene family including poly-para-xylylene, mono-chloropoly-para-xylylene, dichloro-poly-para-xylylene and analogs thereof. The parylene membrane is vacuum deposited on the outer surface of the first membrane in an amount sufficient to occupy the biologically active sites to an extent limiting biological attachment but not significantly affecting the electrochemical performance of the biosensor.

For example, polyurethane membranes have shown some promise as a membrane for glucose sensors. However, the outer surfaces of such membranes have bioactive attachment sites, i.e., oxygen and hydrogen, each of which is well recognized for supporting protein and fibrin attachment. The parylene polymers used in the present invention are phenyl-based polymers having connecting CH_2 groups. Other similar polymers have connecting -NH- groups, -SH- groups or other limited hydrogen atom donors. These phenyl-based polymers such as poly-para-xylylene, adhere to the underlying surface by hydrogen bonding between the connecting CH_2 groups and an oxygen, fluorine, chlorine, or other electron donor on the base membrane substrate. Such hydrogen bonding leaves only the phenyl rings exposed to the surrounding milieu, and thus precludes attachment sites from circulating proteins or cells that would otherwise attach thereto, thereby degrading the sensitivity and accuracy of the electrochemical reaction and resultant signal.

As set forth in greater detail below, a biosensor employing an improved membrane in accordance with the present invention, when implanted in-vivo and removed for testing, yielded a membrane without protein or fibrin attachment. Pre-implant readings and post-implant readings showed a high degree of correlation. In contrast, an uncoated control sensor membrane was occluded with fibrin and protein attachment so as to preclude post removal readings.

The use of the phenyl ring polymers herein differs from the approach taken in copending application United States Serial Number 346,340 filed on November 28, 1994 and assigned to the assignee of the present invention. Therein a membrane of the parylene family of polymers was used as a semi-permeable membrane to protect cellular moieties from the patient immune system while allowing cell nutrients, chemical signals for the cellular production, and the chemical moiety produced thereby to flow through the membrane. The thickness of the polymer was the prime determinant of membrane porosity and membrane strength and desirable membranes were produced in the 2,000 to 5,000 Angstroms for monolithic membranes. In contrast, the membrane for providing biological passivation in the present invention is an order or orders of magnitudes thinner to produce the desired porosity, generally 1,000 Angstroms or below depending on the base membrane material. Such an ultra thin membrane would normally not have sufficient mechanical strength to withstand the biological forces of implantation. This is achieved in the present invention because the membrane is deposited conformally and preferentially at the attraction sites on the base membrane, rather than by the cross linking network of only the base polymer. In other words, the base membrane functions more or less like a template for the biologically inert membrane until the active sites are

occupied. Depending on the overall properties desired, the coating may be applied in a manner in which only a portion of the sites are bonded to provide the desired biological inertness as needed. The membrane may also be applied in excess to the extent that the desired membrane performance characteristics are not adversely affected.

Accordingly, the present invention provides an electrochemical biosensor for determining the level of a target chemical in a biological fluid wherein an electrochemical system includes a substrate which reacts with the target chemical to yield a system signal related to the concentration in the biological fluid of said target chemical. A first membrane on the biosensor immobilizes the substrate and has a porosity permitting passage therethrough of the target chemical to react with the substrate. The first membrane has a surface exposed to the biological fluid, said membrane being characterized by electron donor sites susceptible to facilitating attachment thereon of proteins and fibrin, thus impairing the system signal. A second membrane is bonded to the electron donor sites of said first membrane. The second membrane is formed of a phenyl-based polymer having connecting hydrogen atom donors which bond to the electron donor sites at least sufficiently to form an outer surface on the first membrane exposed to the biological fluid without significantly changing the porosity provided by the first membrane.

Further, the present invention provides a biologically inert membrane composite substrate including a first membrane characterized by a predetermined porosity and formed of a material with biologically active surface sites capable of supporting protein and tissue attachment when exposed to biological fluids. A second membrane consisting of a phenyl-based polymer having connecting hydrogen donors

is bonded to the biologically active surface sites sufficiently to render such sites biologically inert without significantly affecting the predetermined porosity of the first membrane.

Moreover, the present invention provides a method for biologically passivating a membrane having a porosity permitting passage therethrough of a chemical in a biological fluid and a surface with attractive sites for proteins and fibrin, wherein a phenyl-based polymer having connecting hydrogen bond donors is bonded to the attractive sites in an amount sufficient to render the surface biologically inert but insufficient to impair passage through said membrane of said chemical.

BRIEF DESCRIPTION OF THE DRAWINGS

The above and other features and advantages of the present invention will become apparent upon reading the following detailed description of the preferred embodiments taken in conjunction with the accompanying drawings in which:

Figure 1 is a diagrammatic drawing of a biosensor in accordance with the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Referring to the drawings for the purpose of describing preferred embodiments of the present invention, Figure 1 is a diagrammatic view of an electrochemical biosensor **10** for determining the levels of chemicals in biological fluids. The embodiments are described with reference to an implantable glucose sensor for determining the concentration of glucose in blood sera. However, it will be appreciated that electrochemical biosensors for determining the presence of other target chemicals in fluids including oxygen, potassium, calcium, acid, base, protons, CO_2, sodium, chloride and the like are within the scope of the

features and advantages provided by the present invention.

The biosensor **10** may take any recognized form such as disclosed in the aforementioned Gough et al. publication and will be described with reference to the model set forth in Gough et al., Diabetes Care, Vol. 5, No. 3, May-June 1982, pp. 190-198, which is incorporated herein by reference. Therein, the biosensor **10**, immersed in a biological fluid **11**, comprises an oxygen electrode **12** covered by a base membrane **14** containing an immobilized enzyme layer **16**. The enzyme layer **16** comprises glucose oxidase and catalase. In the presence of glucose and oxygen, the electrode **12** produces a glucose-modulated, oxygen dependent current. It will be appreciated that this layer is not limited to an enzyme per se but in other applications may be any compound that reacts with another compound in a predictable and quantitatively measurable manner; or in other words, a specific binding pair. The enzyme layer **16** is separated from the electrode **12** by a hydrophobic, oxygen-permeable layer **18**. The membrane is formed of a biocompatible material such as polyurethane with a permeability that restricts access of macromolecules to the underlying layers. The layer **18** is a hydrophobic, oxygen-permeable membrane that prevents electrode fouling due to the hydrophilic electroactive molecules in biological fluids. A spacer **20** separates the electrode **12** from a counter electrode **22**. The electrodes **12** and **22** are connected to an electrical system **23** by leads **24** and **26** and delivering thereto a current flux related to the electrochemical reactions within the biosensor. Additionally, the electrical system is connected to a reference electrode **28**. As discussed in greater detail in the above publication, the system **23** outputs information related to the concentration of glucose in the biological fluid. The various laminae are enclosed

by a housing, not shown. In the present invention, the outer surface of the base membrane **14** is covered by a biologically inert membrane **30**.

As mentioned above, various materials have been proposed for biosensor membranes. Among the more prevalent membranes are polyurethane, cellulose acetate, perfluorosulfonic acid polymer and others well known in the art. Many of these materials are biocompatible in that the materials do not induce inflammation when implanted. However, these materials have well-recognized bioattractive sites that for proteins and fibrin facilitate a biological overgrowth that results in a progressive reduction in sensing area and resultant drift in electrical signal, ultimately leading to complete blockage of the membrane and loss of meaningful signal. These attractive sites typically have repeating electron donor sites including oxygen, fluorine, chlorine and the like.

In the present invention, the biologically inert membrane **30** is formed of a material characterized by a phenyl-based polymer having connecting hydrogen donors that bond to the biologically active sites, thereby presenting to the biological fluid **11** a surface comprised of non-reactive phenyl rings. A preferred membrane material is selected from the parylene family of polymers, including poly-para-xylylene, mono-chloro-para-xylylene, dichloro-para-xylylene and analogs thereof. The parylene polymers have connecting CH_2 groups. Other similar polymers have -NH- groups, -SH- groups and other limited hydrogen atom donors. These polymers bind to the active sites on the base membrane polymer through hydrogen bonding at the connecting groups. This is generally achieved with an ultra thin layer of the inert membrane material, typically 1000 Angstroms or less, and generally between 50-500 Angstroms. At this thickness, the material, vacuum deposited in the case of the parylene polymers,

is applied preferentially to the active sites on the base polymer and believed substantially to the exclusion of cross linking with itself in a manner which renders the composite membrane biologically inert without affecting the desired membrane properties, such as permeability and porosity.

It does not appear necessary that the membrane 30 completely passivate all the active sites. There may be instances where a less than complete coating will provide biological protection sufficient for the membrane application. Also, the membrane may be applied in excess of the amount needed for inertness. However, the thickness should be controlled to prevent a diminution of membrane performance.

The aforementioned membrane thus provides biological passivation without a diminution of sensor sensitivity as demonstrated by the following examples.

Example 1

A pCO_2 membrane (available from NOVA Biomedical, Waltham MA as catalog no. 07543) was coated with about 500 Angstroms of poly-para-xylylene to form a second membrane thereon. The coated membrane was tested in RPMI media on a NOVA Stat Profile 5 blood gas analyzer which combines blood gas and related stat tests of serum, plasma, whole blood and expired gas for in vitro diagnostic use. The biosensor was tested in 7 consecutive trials and indicated pCO_2 levels of 32.04 STD 1.15. A similar not coated membrane was tested in 6 consecutive trials and indicated pCO_2 levels of 28.63 STD 5.96. It is thus apparent that second membrane did not affect biosensor readability and reliability.

Example 2

A pO_2 Membrane (available from NOVA Biomedical, Waltham MA as catalog no. 11099) was coated with about 500 Angstroms of poly-para-xylylene to form

a second membrane thereon. The coated membrane was tested in RPMI media on a NOVA Stat Profile 5 blood gas analyzer which combines blood gas and related stat tests of serum, plasma, whole blood and expired gas for in vitro diagnostic use. The biosensor was tested in 7 consecutive trials and indicated pO_2 levels of 247.94 STD 4.44. A similar not coated membrane was tested in 6 consecutive trials and indicated pO_2 levels of 251.41 STD 16.39. As in the first example, it is thus apparent that second membrane did not affect biosensor readability and reliability.

Example 3

A glucose membrane (available from NOVA Biomedical, Waltham MA as catalog no. 08469) was coated with less than about 500 Angstroms of poly-para-xylylene to form a second membrane thereon. The coated membrane was tested in a NOVA Stat Profile 5 blood gas analyzer which combines blood gas and related stat tests of serum, plasma, whole blood and expired gas for in vitro diagnostic use. The biosensor was tested in 8 consecutive trials and indicated glucose levels of 207.7 mg% STD 1.59. A similar uncoated membrane was tested in 10 consecutive trials and indicated glucose levels of 200.5 mg% STD 1.59. It is thus apparent that second membrane did not affect biosensor readability and reliability.

Thereafter the coated membrane and the uncoated membrane were implanted into a 4 kg New Zealand White rabbit with the membranes exposed subcutaneously. The membranes were removed after 21 hours. The uncoated membrane was occluded and overgrown with tightly adhering hematocrit which was not dislodged by repeated washings and had to be physically removed for testing. The membrane was tested in 8 trials and indicated glucose levels of 188.25 mg% STD 5.07. The coated membrane was

essentially clear of any fouling and was readily washed in normal saline solution. The coated membrane was tested in 8 trials and indicated glucose levels of 207.25 mg% STD .7. The foregoing indicates that the uncoated membrane was adversely affected in short term implant due to biofouling whereas the membrane coated in accordance with the present invention was not subject to biofouling and did not experience any diminution in signal.

In addition to the aforementioned applications, it will be apparent to those skilled in the art that the composite membrane may be used in other biological applications wherein it is desired to protect cellular and chemical moieties from biological fouling while providing desired porosity and diffusions. Examples of such applications include indwelling chemical sensors, indwelling electrical sensors, long term drug delivery carriers that must be free from fibrin or protein occlusion to release their active ingredients or release the active agent in response to a stimulating moiety found in vivo.

While the present invention has been described with the detection of chemical and biological substances that are normally, abnormally, or pathologically present in the blood or other physiological fluids, and whose detection may be desired on a continuing basis, these chemical or biological substances may be naturally occurring within the subject in which the biosensor is implanted, or by unusual occurrence because of disease or reaction to physiological stress. Examples of such chemical and biological substances include, but are not limited to, hormones, peptides, proteins, glycoproteins, triglycerides, fats, lipids, polysaccharides, carbohydrates, vitamins, minerals, therapeutics, and metals.

As used herein, a "hormone" is defined as a biological substance secreted by a specific tissue, and includes those substances having activity at a different site than the site of secretion and precursors thereof, and substances having activity at the site of secretion (sometimes called autocoids), and secreted by the pituitary gland (or adenohypophysis), and specifically include the growth hormones (GH), melanocyte-stimulating hormones, somatomedins, and lipotropins.

The biosensor of the present invention may also be useful in the detection of compounds that are normally found within the brain and which secrete neurologically active substances. Therefore, the detection of neuropeptides may be provided in the practice of the invention, including the detection of neuropeptide families of the endorphins, the glucagon-secretins, and the substance-P neuropeptides. Endorphins include the proopiomelanocortins, the proenkephalins, the prodynorphins and hormones derived therefrom. The glucagon-secretins include glucagon, vasoactive intestinal polypeptide (both found in pancreatic islets), secretin and growth hormone releasing factor (GHRF). The substance-P neuropeptides include vasotocin, vasopressin and oxytocin. It is specifically intended that the detection of substances secreted by single large clusters of neurons (such as oxytocin, vasopressin, LHRH, GHRH, and proopiomelanocortin) are embraced by the scope of the invention, as well as the detection of substances secreted by cells normally distributed throughout the brain (such as somatostatin, cholecystokinin and enkephalin).

The continuing detection of vitamins present in blood and other fluids is another aspect of the invention. This aspect is particularly useful in monitoring vitamin levels in subjects who are at risk

for vitamin deficiencies. Such vitamins include vitamin A, thiamine, riboflavin, nicotinic acid, vitamin B_6, vitamin D, iron, folic acid, and vitamin B_{12}. The detection of vitamins via their reactions with specific enzymes is known. For example, the presence of thiamine can be detected by its reaction with the enzymes erythrocyte transketolase (ETK) and thiamine pyrophosphate (TPP). Similarly, the presence of riboflavin may be detected by its known reaction with erythrocyte glutathione reductase (EGR). Vitamin B_6 may be detected by its reaction with erythrocyte glutamic-oxaloacetic transaminase (EGOT), and vitamin D may be detected by its reaction with serum alkaline phosphatase.

Antibodies which may be detected by the biosensor of the present invention include those of the immunoglobulin family, including IgA, IgD, IgE, IgG and IgM. The detection of other immunological compounds and cells are a further aspect of this invention. These other immunological compounds and cells include interleukins, cytokines, major histocompatibility complexes (MHC), T cells, complement, and macrophages.

The presence of drugs, other therapeutics and their metabolites may be detected by the biosensor of the present invention by known individual reactions with drug-specific enzymes and other reactive compounds. By drugs is meant any pharmaceutical with an intended and known therapeutic or diagnostic value, but may also mean an illegal or controlled substance whose detection is desired for forensic or monitoring reasons.

The present invention is concerned primarily with the treatment of human subjects, but may also be employed for the treatment of other mammalian subjects, such as cows, pigs, goats, cats, and dogs, for veterinary purposes, or where compounds detected by the

biosensor are being produced in the animal for subsequent collection and the like.

One embodiment of the invention is the use of an electrobiochemical biosensor to detect substances such as hormones, glucose, drugs, and the like in animals, for veterinary and/or agricultural purposes. As an example, growth hormones are sometimes administered to an animal subject for the purpose of increasing meat production. However, at excessively high concentrations, such a hormone may cause deleterious effects in the consumer. A biosensor provided by the present invention which comprises a substrate reactive with such a hormone may therefore be implanted in such a meat-producing animal to provide a means of monitoring such levels on an ongoing basis.

Various modifications of the above described embodiments will be apparent to those skilled in the art. Accordingly, the scope of the invention is defined only by the accompanying claims.

WHAT IS CLAIMED IS:

1. An electrochemical biosensor for determining the level of a target chemical in a biological fluid, said biosensor comprising:

an electrochemical system including a substrate which reacts with the target chemical to yield a system signal related to the concentration in the biological fluid of said target chemical;

a first membrane immobilizing said substrate and having a porosity permitting passage therethrough of the target chemical to react with said substrate said first membrane having a surface characterized by electron donor sites susceptible to facilitating attachment thereon of proteins and fibrin,thus impairing said system signal; and

a second membrane bonded to said electron donor sites of said first membrane, said second membrane being formed of a phenyl-based polymer having connecting hydrogen atom donors, said hydrogen atom donors bonding to said electron donor sites of said first membrane at least sufficiently to form an outer surface on said first membrane without significantly changing the porosity provided by said first membrane, wherein said outer surface is exposed to the biological fluid and consists of phenyl rings.

2. A biologically inert membrane composite substrate, comprising:

a first membrane characterized by a predetermined porosity and formed of a material having biologically active surface sites capable of supporting protein and tissue attachment when exposed to biological fluids; and

a second membrane consisting of a phenyl-based polymer having connecting hydrogen donors bonded to said biologically active surface sites sufficiently

to render said sites biologically inert without significantly affecting said predetermined porosity of said first membrane.

3. A method for biologically passivating a membrane having a porosity permitting passage therethrough of a chemical in a biological fluid and a surface with attractive sites for proteins and fibrin, comprising applying to said membrane a phenyl-based polymer having connecting hydrogen bond donors bonded to said attractive sites in an amount sufficient to render said surface biologically inert but insufficient to impair passage through said membrane of said chemical.

4. An electrochemical biosensor according to Claim 1, wherein said phenyl-based polymer is a parylene polymer.

5. An electrochemical biosensor according to Claim 1, wherein said phenyl-based polymer is selected from the group consisting of poly-para-xylylene, mono-chloro-para-xylylene and dichloro-para-xylylene.

6. An electrochemical biosensor according to Claim 1, wherein said second membrane has a thickness of less than about 1000 Angstroms.

7. An electrochemical biosensor according to Claim 1, wherein said second membrane has a thickness of between about 50 and about 500 Angstroms.

8. An electrochemical biosensor according to Claim 1, wherein said target chemical is glucose.

9. An electrochemical biosensor according to Claim 1, wherein said substrate comprises glucose oxidase.

10. A biologically inert membrane composite substrate according to Claim 2, wherein said phenyl-based polymer is a parylene polymer.

11. A biologically inert membrane composite substrate according to Claim 2, wherein said phenyl-based polymer is selected from the group consisting of poly-para-xylylene monochloro-para-xylylene and dichloro-para-xylylene.

12. A biologically inert membrane composite substrate according to Claim 2, wherein said second membrane has a thickness of less than about 1000 Angstroms.

13. A biologically inert membrane composite substrate according to Claim 2, wherein said second membrane has a thickness of between about 50 and about 500 Angstroms.

14. A method according to Claim 3, wherein said phenyl-based polymer is a parylene polymer.

15. A method according to Claim 3, wherein said phenyl-based polymer is selected from the group consisting of poly-para-xylylene, mono-chloro-para-xylylene and dichloro-para-xylylene.

16. A method according to Claim 3, wherein said phenyl-based polymer is applied to said membrane by vacuum deposition.

17. A membrane for providing biological passivation, said membrane comprising a phenyl-based polymer.

18. The membrane of Claim 17 wherein said phenyl-based polymer is selected from the group consisting of polyphenyl, poly-para-xylylene, mono-chloro-para-xylylene and dichloro-para-xylylene.

19. The membrane of Claim 18, wherein said polymer has connecting groups selected from the group consisting of H, CH_2, SH, and NH.

20. The membrane of Claim 19, wherein said membrane has a thickness of less than about 1000Å.

21. A method for protecting cellular and chemical moieties from biological fouling comprising surrounding said moieties with a membrane comprising a phenyl-based polymer.

22. The method of Claim 21 wherein said phenyl-based polymer is selected from the group consisting of polyphenyl, poly-para-xylylene, mono-chloro-para-xylylene and dichloro-para-xylylene.

23. The method of Claim 22, wherein said polymer has connecting groups selected from the group consisting of H, CH_2, SH, and NH

24. The method of Claim 23, wherein said membrane has a thickness of less than about 1000Å.

25. A cellular or chemical moiety which has been coated with a membrane, said membrane comprising a phenyl-based polymer.

26. The moiety of Claim 25 wherein said phenyl-based polymer is selected from the group consisting of polyphenyl, poly-para-xylylene, mono-chloro-para-xylylene and dichloro-para-xylylene.

27. The moiety of Claim 26, wherein said polymer has connecting groups selected from the group consisting of H, CH_2, SH, and NH.

28. The membrane of Claim 27, wherein said membrane has a thickness of less than about 1000Å.

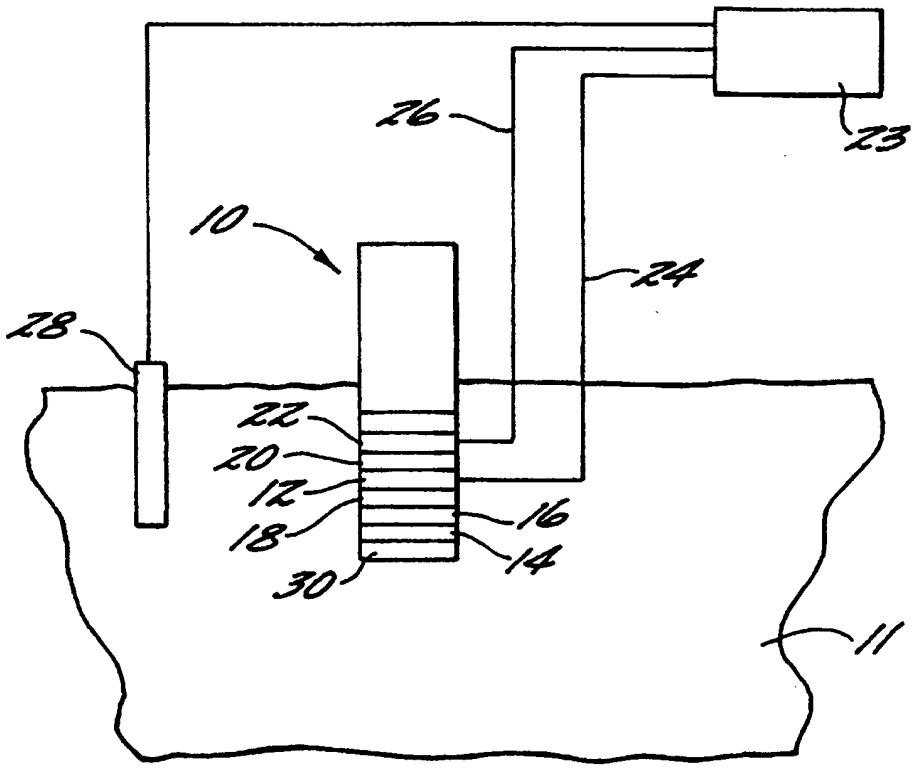

Fig. 1.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 97/08648

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N27/327 C12Q1/00 G01N33/543 B01D71/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12Q G01N B01D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ELECTROANALYSIS, vol. 6, no. 5/6, May 1994, pages 423-429, XP002040030 D. CENTONZE ET AL: "Permeation of solutes through an electropolymerized ultrathin poly-o-phenylenediamine film used as an enzyme-entrapping membrane." see the whole document ---	1-3,17, 21
X	EP 0 259 109 A (ADVANCED POLYMER TECHNOLOGY) 9 March 1988 see the whole document ---	2,3,17
X	US 5 151 183 A (SEDATH ROBERT H ET AL) 29 September 1992 see the whole document ---	2,3,17
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[X] Further documents are listed in the continuation of box C.

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1

Date of the actual completion of the international search	Date of mailing of the international search report
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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
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(57) Abstract

A system for transferring binary medical files from remote devices to a central database over the internet includes an adapter for converting the binary medical information file to a compatible file of keystroke codes. The keystroke codes are transferred to a computer which converts the codes to ASCII characters which are input by an applet and transferred to the central database. Software at the central database recovers the original binary medical information file. Additionally, a system for accessing medical reports in real–time utilizes a report requesting page having a form for entering ID codes and report requesting data. The codes and data are transferred over the internet to a host computer which generates a report file and transfers the file via the internet to the requestor to be displayed on a computer.

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SYSTEM FOR DOWNLOADING AND REPORTING MEDICAL INFORMATION

BACKGROUND OF THE INVENTION

Medical Monitoring Devices

Various medical monitoring devices exist that download medical measurement data from a remote location to a central location. Such systems require a specialized interface to connect the device to a communication system such as the public telephone system or a pager information system.

For example, the AIRWATCH respiratory function monitor, described in U.S. Patent Application No. 5,549,117 ("the '117 patent") filed May 23, 1994 and assigned to the assignee of the present application, is a hand-held respiratory monitor that stores a binary file including information relating to respiratory parameters. When the AIRWATCH is connected to a telephone line a connection is automatically established to a central database and the encoded file is modulated by a software modem into analog signals which are transferred to a modem at the central site. The central modem demodulates the signals and generates a file which is processed at the central location and used to update a data base.

Other medical devices include interface software and hardware connections to a personal computer. The computer can then be used to communicate with the central data base utilizing a modem.

Additionally, as more monitoring devices are utilized in a patient's home various devices could be located in rooms or locations. Accordingly, the problems of interfacing to the central database are compounded.

The remote connection of medical devices, such as the AIRWATCH, via the public telephone lines presents problems when such devices are to be used worldwide. The binary

medical information file may include information related to glucose levels, blood pressure, etc. The public telephone systems of various countries are not standardized so different models would have to be built for different countries thereby increasing the overall cost of manufacturing the devices. Since low cost is critical to encourage widespread use of such devices the lack of telephone system compatibility is a serious problem to the internationalization of the technology.

Additionally, each device generally includes a front end to communicate results of a measurement to the user of the device, e.g., a patient or health care provider. Typically, a front end includes LEDs, a alpha-numeric display, synthetic voice output etc. The device may be coupled to a personal computer which would execute special software to operate as a front end.

Report Distribution System

A system for generating and distributing medical reports from a central database is described in the above-referenced patent application. Various formats including graphs and tables are described. Typically, these reports are delivered by fax, mail, or e-mail. However, none of these delivery systems facilitate real-time access of medical records by a requestor.

SUMMARY OF THE INVENTION

In one aspect of the present invention, the world-wide-web (WWW) is utilized as a universal front end for a medical monitoring device. Information from the device is communicated to a personal computer executing standard web browser software. A CGI form or applet, executed by the web browser software, receives the communicated information and functions as the front end of the device. Thus, a high-resolution personal computer display can be utilized as the front end of an inexpensive medical device.

According to another aspect of the invention, the WWW front-end includes a hot link to a personal physician or other health-care provider. The link includes a URL to a web

page of the doctor and transmits the medical information downloaded from a medical device.

According to another aspect of the invention, medical information received by the personal computer is communicated to the central database over the internet.

According to another aspect of the invention, an adapter formats the output of a medical device into an input format the can be processed by a page displayed by a web browser or by an applet executed by the web browser.

According to another aspect of the invention, medical reporting devices in different locations can be connected utilizing a home health-care bus. The devices can be coupled to the electrical wiring which is used to communicate information downloaded by the various devices to a central data handler.

According to one aspect of the present invention, a system is provided for utilizing the internet to transfer binary medical files between a remote health parameter monitoring device and a central database. Since the internet is platform independent it facilitates the standardization and internationalization of health monitoring systems.

According to a further aspect, a convertor is connectable to the device to receive a binary medical information file and convert the file to key codes to form a compatible medical information file. The key codes are transferred to a computer to be processed as keystroke data.

According to a still further aspect, a client workstation attached to the internet utilizes a browser to display a data transfer page embedding a data transfer applet. The data transfer applet accesses a keyboard buffer to input the encoded compatible file and transfer the encoded compatible file over the internet to the central database.

According to a still further aspect of the invention, the received encoded compatible file is decoded and decompatible at the central data base to recover the original binary medical information file.

According to another aspect of the invention, real-time access to medical reports is provided over the internet.

According to a further aspect, a report home page includes a form for accepting ID codes and report format information. The request information entered into the form is transferred over the internet to a request delivery server application operating on a host computer utilizing the common gateway interface (CGI) or an applet.

According to a further aspect of the invention, the report delivery software invokes report generating software at the central data base to generate the requested report in the form of either a text or graphics report file. The request delivery software formats the report file and transfers the formatted report file via the internet to the requestor to be displayed at the requestor's computer.

In one aspect of the present invention, the world-wide-web (WWW) is utilized to provide an enhanced interface to a medical monitoring device. Information from the device is communicated to a personal computer executing standard web browser software. A CGI form or applet, executed by the web browser software, receives the communicated information and functions as the front end of the device. Thus, a high-resolution personal computer display can be utilized as the front end of an inexpensive medical device. A result page generated by web server functions as the display of the medical measurement device. Additionally, the web page includes applets for controlling the device according to standard input, e.g, via mouse or keyboard, which is processed by the result page.

According to another aspect of the invention, medical reporting devices in different locations can be connected utilizing a home health-care bus in the form of the "Universal Serial Bus" (USB).

According to another aspect of the invention, a serial ID code is transferred to a remote data base server. The data base server responds to the code by providing data associated with the code. User specific data accessed by the

ID code is utilized to format the response for the particular user.

Other features and advantages of the invention will be apparent from the following detailed description and appended drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1A is a schematic diagram of first preferred embodiment of the invention;

Fig. 1B is a block diagram of a personal computer;

Fig. 2 is a flow-chart depicting the steps for using a web browser as a front end of a medical measurement device;

Fig. 3 is a schematic diagram depicting a home health-care bus;

Fig. 4A is a schematic diagram of a medical measurement device that downloads data to computer through an adapter;

Fig. 4B is a flow-chart depicting the steps of converting a medical information file into a format compatible with a standard input to a personal computer;

Fig. 5 is a diagram depicting a standard keyboard interface;

Fig. 6A is a schematic diagram of an adapter;

Figs. 6B and 6C are diagrams depicting a specific embodiment of an adapter;

Fig. 7 is a flow-chart depicting the steps of transferring a compatible medical information file over the internet;

Fig. 8 is a schematic diagram of a system for transferring medical reports over the internet; and

Fig. 9 is a flow-chart depicting the steps of transferring medical reports over the internet.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Fig. 1A is a block diagram of a preferred embodiment of virtual front end utilizing standard web-browser software. In Fig. 1A, a medical device 10 includes an infrared (IR) transmitter for transmitting medical measurement data, modulated onto an IR carrier, to the IR input of a personal computer 30. In the following the term personal computer will be utilized to refer to any device, such as WebTV or other web appliances, that can be used to access the internet. The transmitted medical measurement data is transmitted in the form of keyboard data (as described more fully below) before being modulated onto the IR carrier. The IR transmitter and IR keyboard interface are standard, well-known parts and are not part of the present invention. The IR keyboard interface directly serves a variety of input devices such as, for example, a keyboard, mouse, AIRWATCH, thermometer, range of motion sensors, barcode reader, scale, height measurement, blood pressure cuff, tympanic compliance, mag stripe writer, tag writer, printer, and printer for wrist band.

Fig. 1B is a block diagram of a typical personal computer and connected peripheral device. The CPU executes programs which may be provided from the hard-disk drive (HDD), floppy-disk drive (FDD), from the serial port, or from other sources. Typically, a computer is connected to the internet via a modem connected to the serial port.

The personal computer executes standard web-browser software, e.g., Netscape Navigator, America On Line, or MicroSoft Internet Explorer. The World Wide Web (WWW) is a network for connecting computers via the internet. Typically, a client computer executes a browser application that allows a user to access documents from any site on the WWW. Documents in hypertext mark-up language (HTML) include links to other HTML documents, graphics and sound files, executable applications, etc. In some cases an HTML document includes executable code, scripts, embedded within the document. In other situations an applet, for example a Java applet, is referenced within an HTML document and downloaded from a server to execute on the client computer displaying the HTML document with the browser application.

Forms may be included in HTML pages. Data is entered into a form through the keyboard and transmitted to a server application utilizing the common gateway interface (CGI). A program resides on the server that receives the information from the form and returns appropriate data. The types of information that can be exchanged includes text data and binary files such as GIF images.

In one embodiment, depicted in the flow-chart of Fig. 2, a front-end home page is displayed by the web-browser. The URL of the front-end home page can be stored as a bookmark or favorite place.

The compatible medical data is accepted by a form included in the front-end home page and transmitted to a server application executing on a host computer 32 (Fig. 1A) using the common gateway interface (CGI). The server application generates a page displaying the test results and transmits the test results page to the web-browser. The web-browser then displays the results to the user.

Alternatively, the compatible medical data can be input to a Java applet executed by the browser software. The Java applet formats a results image which is displayed by the web-browser. In the interest of security, the I/O of a Java applet is restricted. For example, Java applets cannot read or write files on the client computer executing the applet. Additionally, the browser application limits an applet's network connectivity. An applet's network connectivity is currently limited to its host machine. However, a Java applet can input keyboard data entered through the keyboard of the client machine.

Regardless of whether the results page is generated by the server or a Java applet, the results page can include a hot link to the web page of a personal physician or other health-care provider. By clicking on the link the results of a medical measurement is transmitted over the internet to the physician's computer 34 (Fig. 1A). A internet link between the computers 30 and 34 of the patient and physician facilitates real time-health care monitoring. For example, after reviewing the results of a measurement the physician

might suggest retrying measurement under the same or different conditions.

Additionally, as depicted in Fig. 1A and described more fully below, the compatible medical data can be transmitted to the central database 36 (Fig. 1A) utilizing the CGI or a Java applet. The compatible medical data is received at the server which decodes the compatible medical data and transfers the decoded data to a central database 36 which integrates the decoded data into the database 36.

In Fig. 1A, a device utilizing an IR transmitter is depicted. If the device were in a different room than the user's computer then the device could not transmit data because IR transmission is limited to line-of-sight. Accordingly, if the device were heavy or immobile, such as a scale, or if multiple devices were located throughout the home an IR interface to the computer would not be practical.

However, as depicted in Fig. 3, various medical measurement devices throughout the home can be connected to a home healthcare bus. In a preferred embodiment, information from each device 10A and 10B is coupled to the home wiring system 300 and is transmitted to a data center 302 via the wiring system. The data is transmitted over the home wiring system utilizing interfaces well-known in the art. Alternatively, special wires, cable, IR repeaters, radio-frequency, or fiber could be utilized to form the bus. The data center 302 includes an interface, for example an IR transmitter, for providing encoded keyboard data to the personal computer.

Alternatively, the medical devices, web appliance, telephone, and other peripheral are connected to the "Universal Serial Bus" (USB). The USB provides a standard to merge desktop connections. USB compliant medical monitors 10A and 10B have USB interface connectors, e.g., the type B connector is identical in size to an RJ-11 socket. The monitors is connected directly to any USB computer or web appliance through a generic cord.

As described in the above-referenced '117 patent, the medical measurement device may be interface to the

telephone line via a reported device which formats measured data and interfaces with the central data base. In the USB embodiment, the reporter may function in two modes.

In a first mode, the monitor downloads measurement data and the reporter interfaces with the central database through the USB bus. In the second interactive mode, the reporter establishes a live connection between the monitor and central server. This allows the reporter to be generic and the server interrogates the monitor directory. The reporter does not need to know anything specific about the particular connected monitor and the server can then be continuously extended to talk to new devices without changing the reporter.

The device of Fig. 1A outputs medical information data encoded as keyboard data which can be received by the keyboard interface of the personal computer. Thus, the medical device could generated medical measurement files in format compatible with a keyboard or other PC input port. Alternatively, medical information data in binary or any other incompatible format could be output by the device to an adapter. The adapter is designed to convert the data output by the device to encoded keyboard data which can be received by the keyboard interface of the computer. A system utilizing an adapter will now be described. In the following the adapter is a stand-alone device which is connected to the output of the medical measurement device. Alternatively, the adaptor could be integrated into the device.

Fig. 4A is a system level diagram of another preferred embodiment of the invention. In Fig. 4A, a medical monitoring device 10 outputs a binary medical information file. As described below, this file may be in the form of analog signals modulated on a carrier frequency or as a digital signal output by a digital interface.

The operation of the system will now be described with reference to Fig. 4A and flow chart of Fig. 4B. The binary file is transferred to an adapter 400 which receives the binary file and converts the file into a compatible medical file in a format that may be processed and decoded by the standard keyboard interface of a personal computer 30. In

the compatible medical file each byte of the medical file is replaced by a scan code comprising ASCII characters which are written to a keyboard buffer as an compatible medical information file. Thus, there is a correspondence between words in the binary medical file and ASCII characters which are stored in the keyboard buffer.

The patient's personal computer 30 is connected to the World Wide Web on the Internet and executes a browser application. An applet or CGI form, invoked by the browser application, reads keystroke ASCII codes from the keyboard buffer and transfers the ASCII codes to a server application. The server application processes the received ASCII codes to reconstruct the original binary medical file which is then processed by software at the server to generate a result page to be displayed by the PC 30 or to store the received medical information in a database 36.

The result web page generated by the server can be formatted to function as an enhanced user interface. For example, the AIRWATCH (described above) includes an LED interface for displaying time, date, personal best data,etc., and includes buttons for controlling monitor functions. As monitors get smaller and more complicated the process of controlling each function of the device with small buttons and a small display gets difficult.

However, if the monitor is connected to web, via the USB for example, then the web server can generate a result page for display on web appliance monitor that includes formatted display of the monitor output parameters and software buttons for controlling the monitor function.

As an example, for the AIRWATCH, the personal best and other data are displayed one at a time. The right and left buttons move to the next digit to the right or left. In an enhanced interface the entire line of parameters would be displayed stretching across the result page. With the standard mouse and keyboard interface any digit could be selected directly and a pop out list used to select the desired value.

Once a monitor is connected to the web, the ID code is provided to the server and functions as a hardware key allowing access to the data on the server associated with that device.

The server responds to the ID by checking user-specific data which describes attributes of the user such as age and native language. The server formats a response page in a manner appropriate to the particular user. Viewing preferences can be saved and recalled during a next session.

Hardware key recognition can be utilized in connection with conventional typed in data such as passwords. If a logging monitor is used by more than one family member a "user selector" indicates to the web application which family member's data is to be displayed.

Similarly, when a connection is established from a doctor's office, the database server recognizes the device and the doctor (by his web login). The connection to the database is authorized and information is displayed appropriately.

PC Keyboard Controller and ISR

The structure of the keyboard 500 and keyboard interface 510 for a PC is depicted in Fig. 5. This configuration is well-know and will be only briefly described. When a key is pressed a scan code, in the form of ASCII codes, unique to the key is generated by the keyboard chip 502 and is serially transferred to the keyboard interface 510 by the keyboard cable 520. The serial data is converted to a parallel byte so that the scan code can be processed by the MPU.

The scan codes are received by the PC and translated to ASCII codes utilizing a Keyboard Interrupt Service Routine (ISR) included in the Basic I/O System (BIOS). The ISR is invoked by INT 09 each time a key is pressed and converts keyboard data into information that is useful to the system. This conversion results in the Keyboard ISR placing a two-byte character code into a keystroke buffer in the PC's memory.

Typically, the keyboard ISR in a PC/AT system converts the codes received into System Scan Codes. These System Scan Codes are then compatible into the two-byte

character codes having a low-order byte, called the main byte, and a high-order byte, called the auxiliary byte. The ASCII value of a key-stroke (if any) is always contained in the main byte and the scan code as the auxiliary byte. When a key, such as a function key, edit key, or function key combination, does not have an ASCII value, then the Keyboard ISR sets the main byte to 00h and the auxiliary byte to a special key value.

A BIOS Keyboard Device Service routines provides an interface through which the operating system or application software can interface with the keyboard buffer.

The Adapter

Fig. 6A is a block diagram of the adaptor 400 which includes a device interface 402, processor 410, and serial interface 420. If the medical device 10m utilizes a modem to output a modulated carrier signal encoding the binary medical file then the device is connected to a modem interface in the device interface 402. If the medical device 10s has a serial output then it is connected to a serial interface in the device interface 402. A specific device interface 402 may have either a modem, serial interface, or combination of the two.

A processing unit 410 converts the words of the binary medical information file to scan codes and transfers the scan codes to the keyboard serial interface 420. The conversion of the words in the binary medical information to scan codes is accomplished utilizing standard techniques, e.g., a look-up-table.

The keyboard serial interface 420 transfers the scan code serially to the keyboard controller on the PC as described above. The keyboard serial interface 420 is a pass-through connection that passes the output from the connected keyboard to the PC when a medical device 10 is not connected to the adapter.

A specific embodiment of a prototype adapter 500 is depicted in Figs. 6B and 6C. In Fig. 6B a device having an output modulated by a modem is coupled to the adapter 500

through a standard RJ-11 jack. A telephone simulator couples the binary medical file to an HP Palmtop computer through a PCM-CIA modem 620. A wedge circuit controllably couples either the keyboard or Palmtop output to the PC.

The operation of the adaptor 500 will now be described for the case where an AIRWATCH respiratory function monitor is coupled to the adaptor. The data interface to the AIRWATCH specifies a 5 byte serial number, a packet list including a header, 128 bytes of packet data, and 2 bytes of CRC (cyclic redundancy checking).

The adapter 500 auto-answers AIRWATCH initiated downloads and send the AIRWATCH data over the IBM PC keyboard prot as if typed on a "virtual" keyboard. Each byte of the AIRWATCH data is converted to 2 ASCII hex nibbles. Thus, for example a byte having hex value 0x1A is represented as if the two-character ASCII string "1A" was typed on the keyboard. In this embodiment the adapter 500 does not perform any CRC or error checking, it simply converts and passes along data that it receives.

As described above, the I/O options of Java applets are limited by security considerations. One such limitation is that the Java output cannot output data through the keyboard interface. For medical devices requiring an acknowledge signal or other handshaking, the adapter is not able to provide the required information. Accordingly, the server application can display an acknowledge which must be provided to the device by the user.

Internet Transfer of Medical Records

Referring to Figs. 1 and 7, a process for transferring medical information from a medical measuring device to a central database 36 will now be described. Referring to the flow-chart of Fig. 7, a browser application, running on the user's computer, utilizes a designated URL to access data transfer page over the internet. As described above, the designated URL may be automatically provided when a medical device 10 is coupled to the adapter 20.

The data transfer page includes an embedded data transfer applet, which in a preferred embodiment is a Java applet. The applet is executed on the user's computer and inputs the converted medical file from the keyboard buffer and transmits the file to the host computer 32.

Alternatively, as described above, the data transfer page can include a form that transmits converted medical data to the host 32 utilizing the CGI.

The host computer host decodes the converted medical file to change the ASCII codes to corresponding bytes of the medical information file.

The medical information file is in a form that is processed by database software to update the medical database 36.

Internet Delivery System

A system for utilizing the internet to deliver medical reports in real-time will now be described with reference to Figs. 8 and 9. Typically, the reports are computer generated from records in a central database and are formatted either as text or graphics files. Additionally, the reports can be formatted as faxes, letters, etc. An example of a central database is described in the '117 patent and includes information downloaded over the telephone system from AIRWATCH devices.

A report requester utilizes a browser executing on a client computer 30 to access a report request page by supplying a designated URL.

The host computer 32 generates a report request HTML document including a FORM to allow feedback from a client computer displaying the report request document using a browser application.

The report requester enters passwords for accessing a particular patient's records. The requestor also indicates the desired format of the report, e.g., a graph, table, or other format. When the requestor completes filling out the form the information entered is transferred to the form

reporting server application executing on the host computer 32 utilizing the common gateway interface (CGI).

A form reporting server application invokes a report delivery script which first checks the codes to confirm that the requester is authorized to access the records. The script then invokes report generating software which generates a report file.

If the report file is a text file then the report delivery script converts the file to an HTML report file an transfers the report file to the client computer to be displayed by the browser application. If the report file is a graphics file it is converted by the report delivery script into a graphics file type that can be displayed by the browser or a browser helper application or plug-in and transfers the compatible graphics report file to the client computer to be displayed by the browser application.

In a preferred embodiment, the report files are Postscript® files which are converted by the server report delivery software to .GIF files before transfer to the client computer. Formats of reports are depicted in the above-referenced patent application.

Alternatively, an interactive requestor user interface can be implemented utilizing a Java applet.

Thus, physicians, health officials, and other medical personnel have real-time access to database records stored at a central location.

The invention has now been described with reference to the preferred embodiments. Alternatives and substitutions will now be apparent to persons of skill in the art. For example, the keyboard interface of a PC has been described. However, the principles of the invention are equally applicable to other platforms including Macintosh® and UNIX. Further, the preferred embodiment utilizes the WWW. Again, other network implementations are within the scope of the invention. Accordingly, it is not intended to limit the invention except as provided by the appended claims.

WHAT IS CLAIMED IS:

1. An adapter for connecting a medical device to a client computer, with the medical device of the type that outputs a digital medical file organized into one or a plurality of words including digital medical measurement data, a modulating system for converting the digital medical file into analog signals for to transmission over the telephone lines to a central location, and with the client computer having a keyboard connector for receiving keyboard input in the form of key codes generated by the keyboard and executing a browser application which displays a data transfer page generated by a host computer and inputs said key codes and transmits the key codes to the host computer, said adapter comprising:

a demodulating unit, coupled to the modulating system of said medical device, for demodulating the transmitted analog signals to recover said digital medical file;

a conversion unit for converting each word of a recovered digital medical file to a corresponding key code;

an interface, connectable to said keyboard connector, for emulating a keyboard and transferring said corresponding key codes to be processed as keyboard data by said client computer so that the data transfer page can input the corresponding key codes and transmit the corresponding key codes to the host computer for processing.

2. A system for connecting a medical device to a central database, said system comprising:

a host computer, connected to a network and executing a server program that receives key codes and converts the codes to corresponding words to reconstruct a digital medical file encoded by the key codes received, and for providing a reconstructed medical file to a central database;

a client computer, connected to a network and having a keyboard connector for receiving keyboard input in the form

of key codes generated by the keyboard and executing a browser application which displays a data transfer page generated by the host computer and that inputs said key codes and transmits the key codes to the server program executing on the host computer;

an adapter for connecting a medical device to a client computer, with the medical device of the type that outputs a digital medical file organized into one or a plurality of words including digital medical measurement data, a modulating system for converting the digital medical file into analog signals for to transmission over the telephone lines to a central location, and with the client computer having a keyboard connector for receiving keyboard input in the form of key codes generated by the keyboard and executing a browser application which displays a data transfer page generated by a host computer and inputs said key codes and transmits the key codes to the host computer, said adapter comprising:

a demodulating unit, coupled to the modulating system of said medical device, for demodulating the transmitted analog signals to recover said digital medical file;

a conversion unit for converting each word of a recovered digital medical file to a corresponding key code;

an interface, connectable to said keyboard connector, for emulating a keyboard and transferring said corresponding key codes to be processed as keyboard data by said client computer so that the data transfer page can input the corresponding key codes and transmit the corresponding key codes to the host computer for processing.

3. An adapter for connecting a medical device to a client computer, with the medical device of the type that outputs a digital medical file organized into one or a plurality of words including digital medical measurement data, a modulating system for converting the digital medical file

into analog signals for to transmission over the telephone lines to a central location, and with the client computer having a keyboard connector for receiving keyboard input in the form of key codes generated by the keyboard and executing a browser application which displays a data transfer page generated by a host computer and inputs said key codes and transmits the key codes to the host computer, said adapter comprising:

a conversion unit for converting each word of an output digital medical file to a corresponding key code; and

an interface, connectable to said keyboard connector, for emulating a keyboard and transferring said corresponding key codes to be processed as keyboard data by said client computer so that the data transfer page can input the corresponding key codes and transmit the corresponding key codes to the host computer for processing.

4. A system for connecting a medical device to a central database, said system comprising:

a host computer, connected to a network and executing a server program that receives key codes and converts the codes to corresponding words to reconstruct a digital medical file encoded by the key codes received, and for providing a reconstructed medical file to a central database;

a client computer, connected to a network and having a keyboard connector for receiving keyboard input in the form of key codes generated by the keyboard and executing a browser application which displays a data transfer page generated by the host computer and that inputs said key codes and transmits the key codes to the server program executing on the host computer;

an adapter for connecting a medical device to the client computer, with the medical device of the type that outputs a digital medical file organized into one or a plurality of words including digital medical measurement data, a modulating system for converting the digital medical file into analog signals for to transmission over the telephone

lines to a central location, and with the client computer having a keyboard connector for receiving keyboard input in the form of key codes generated by the keyboard and executing a browser application which displays a data transfer page generated by a host computer and inputs said key codes and transmits the key codes to the host computer, said adapter comprising:

a conversion unit for converting each word of a digital medical file to a corresponding key code;

an interface, connectable to said keyboard connector, for emulating a keyboard and transferring said corresponding key codes to be processed as keyboard data by said client computer so that the data transfer page can input the corresponding key codes and transmit the corresponding key codes to the host computer for processing.

5. A system for connecting a medical device to a central database, said system comprising:

a host computer, connected to a network and executing a server program that receives key codes and converts the codes to corresponding words to reconstruct a digital medical file encoded by the key codes received, and for providing a reconstructed medical file to a central database;

a client computer, connected to a network and having a keyboard connector configured to receive keyboard input in the form of key codes generated by the keyboard and executing, said client computer for receiving a medical information file from the medical device formatted as key codes and executing a browser application which displays a data transfer page generated by the host computer and that inputs said key codes of the medical information file and transmits the key codes to the server program executing on the host computer.

6. A system for delivering medical reports generated at a central location and utilizing information stored in a central database, said system comprising:

a client computer, connected to a network, executing a browser application displaying a report requesting document for transferring, over the network password information and request format information to a report generating server application;

a host computer, connected to the network, executing said report generating server application, with said report generating server application for invoking report generating software to generate a report file in a browser compatible format, and for transferring the report file to the client computer over the network to be displayed by the browser application executing on the client computer.

7. A system for implementing a universal front-end for a medical measurement device, said system comprising:

a personal computer, connected to a network and including standard I/O ports and a display device;

a data output interface, coupled to a medical measurement device, for providing compatible medical information data including medical information in a digital format compatible with a standard input port of said personal computer;

a processor included in said personal computer, executing web-browser software to display a front-end page and configured to process received medical information data provided by said medical measurement device and to display the results of a medical measurement utilizing the display device.

8. The system of claim 7 where said data output interface provides compatible medical information in the form of key codes compatible with a keyboard interface of a personal computer.

9. A system for providing medical measurement information output by a medical measurement devices to a central database, said system comprising:

a host computer, connected to a network and executing a server program and database software for receiving

medical information data encoded in an output format utilized by web-browser applications, said host computer configured to process received medical information data to enter medical information into said database;

a client computer, connected to a network and including standard I/O ports and a display device;

a data output interface, coupled to a medical measurement device, for providing compatible medical information data including medical information in a digital format compatible with a standard input port of said personal computer; and

a processor included in said personal computer, executing web-browser software to display a data-communication page and configured to process received medical information data provided by said medical measurement device, and to transfer received medical information data over a network to said host computer.

10. A system medical information management system for receiving medical information measured by a plurality of medical measurement devices and providing the information to a personal computer, said system comprising:

a bus, having a plurality of input ports for coupling to one of the medical devices; and

a data collector, coupled to said bus, and including a data output interface, for providing compatible medical information data, including medical information received from each input port of said bus, converted to a digital format compatible with a standard input port of the personal computer.

11. The system of claim 10 wherein:

said bus is the wiring system of a home.

12. A system for implementing a universal front-end for a medical measurement device, said system comprising:

a personal computer, connected to a network and including standard I/O ports and a display device;

a data output interface, coupled to a medical measurement device, for providing compatible medical information data including medical information converted to a digital format compatible with a standard input port of said personal computer;

a processor included in said personal computer, executing web-browser software to display a front-end page and configured to process received medical information data provided by said medical measurement device, to transmit said information over the network to a health-care provider.

13. The system of claim 12 wherein:

said processor is further configured to establish a connection over the network to facilitate real-time communication between a health-care provider and a patient concerning the results of a medical measurement.

14. A system for implementing an enhanced interface for a medical measurement device, said system comprising:

a web appliance, connected to a network and including standard I/O ports and a display device;

a data input/output interface, coupling the medical measurement device and the web appliance, for transmitting compatible information data, from the medical measurement device, in a digital format compatible for processing by said web appliance and for transmitting medical measurement device control information from the web appliance to the medical measurement device;

a processor included in said web appliance, executing web-browser software to display a front-end page and configured to process information data provided by said medical measurement device and to display a result page displaying parameter values relating to the operation of the medical device and for displaying interactive function keys to activate functions in the medical device.

15. A system for implementing a hardware key for a medical measurement device to gain access to a remote database, said system comprising:

a web appliance, connected to a network and including standard I/O ports and a display device;

a data output interface, coupled to a medical measurement device, for providing medical measurement device identification data to said web appliance;

a remote database server coupled to the web, said database server for providing user data when a identification data associated with a user is received;

a processor included in said web appliance, executing web-browser software to display a front-end page and configured to transfer said medical identification data provided by said medical measurement device to said remote database server to gain access to data associated with a user of said medical measurement device.

16. A system medical information management system for receiving medical information measured by a plurality of medical measurement devices and providing the information to a personal computer, said system comprising:

a universal serial bus, having a plurality of input/output ports for coupling to one of the medical devices;

a web appliance coupled to the universal serial bus, with the web appliance with the web appliance including a executing web-browser software to display a front-end page and configured to process information data provided by said medical measurement device and to display a result page;

a telephone connection for connecting a medical device to a remote central data base.

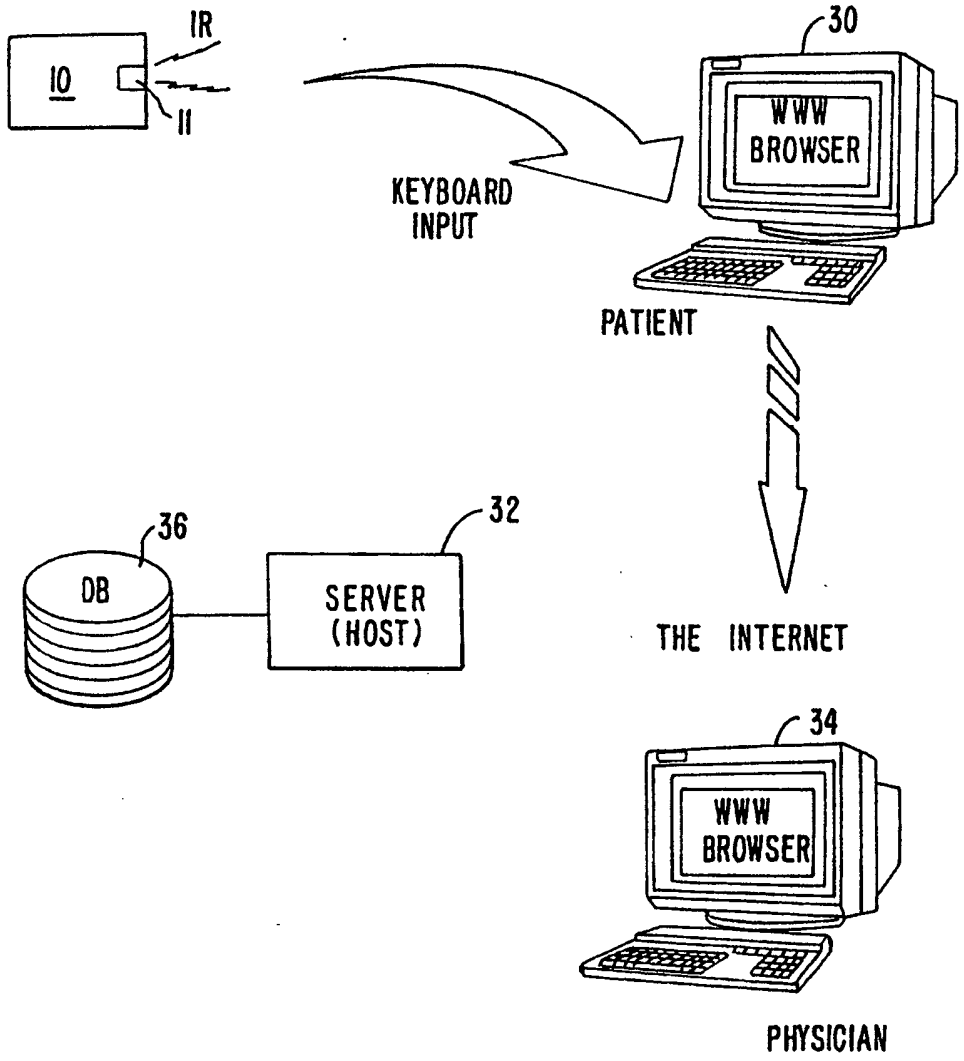
IR
10
11
30
WWW
BROWSER
KEYBOARD
INPUT
PATIENT
36
DB
32
SERVER
(HOST)
THE INTERNET
34
WWW
BROWSER
PHYSICIAN

FIG. 1A.

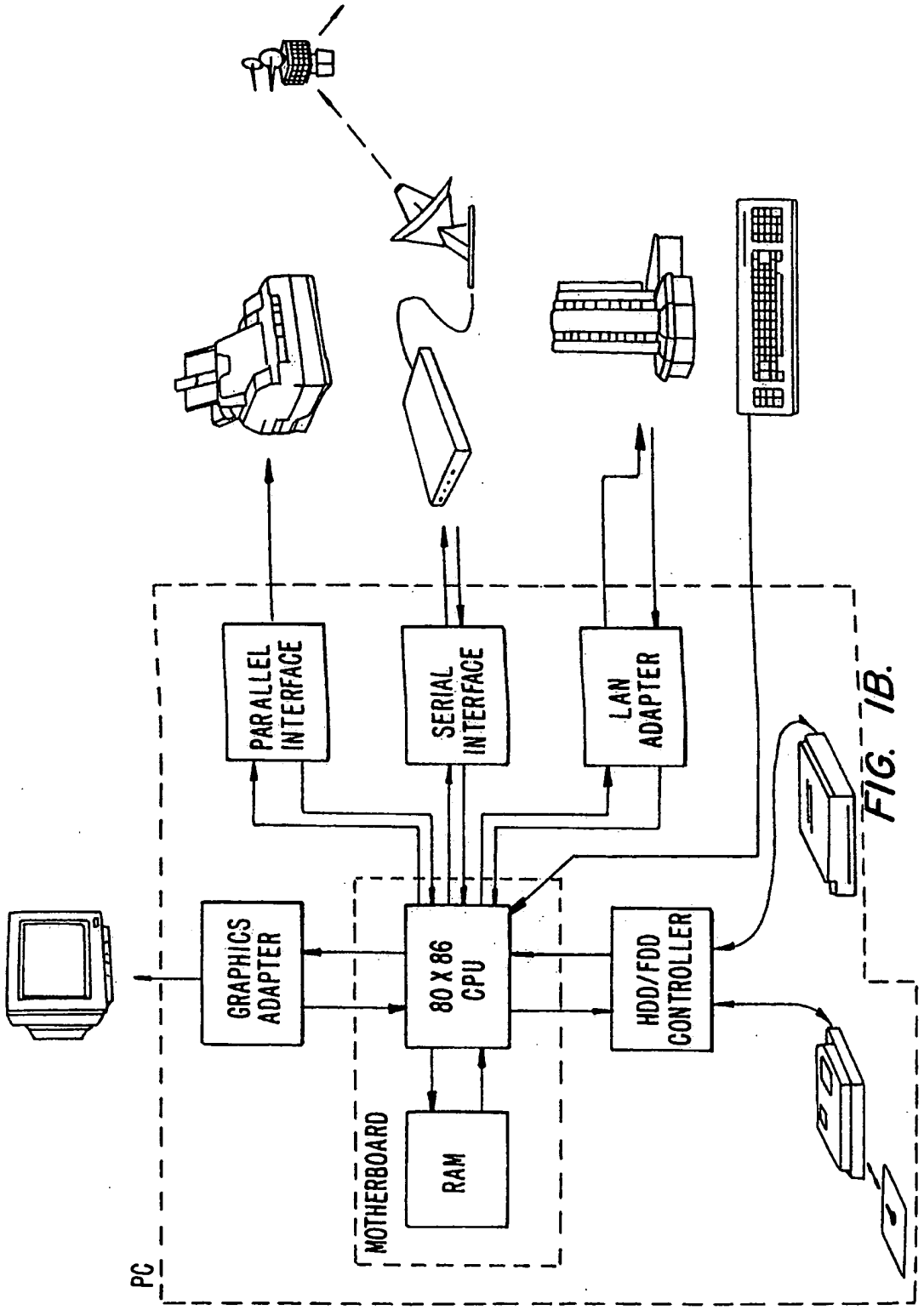
PARALLEL INTERFACE
SERIAL INTERFACE
LAN ADAPTER
GRAPHICS ADAPTER
80 X 86 CPU
HDD/FDD CONTROLLER
RAM
MOTHERBOARD
PC

FIG. 1B.

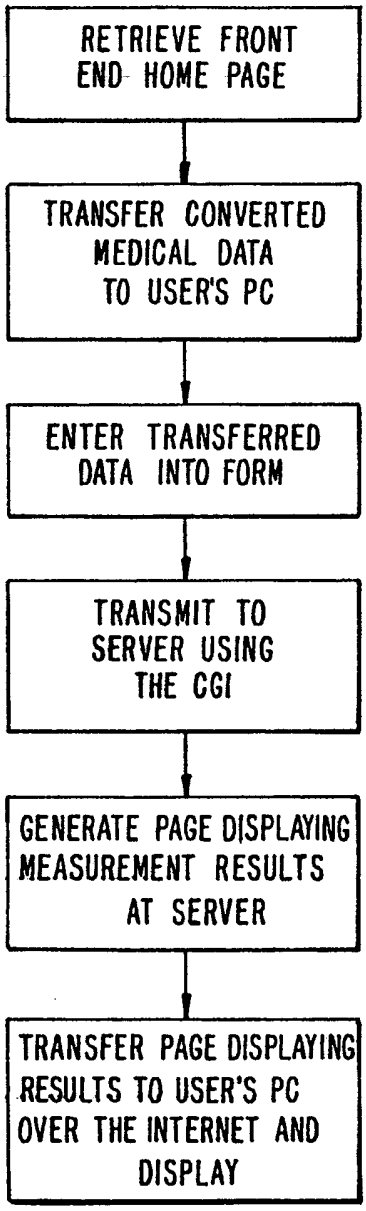
RETRIEVE FRONT END HOME PAGE
TRANSFER CONVERTED MEDICAL DATA TO USER'S PC
ENTER TRANSFERRED DATA INTO FORM
TRANSMIT TO SERVER USING THE CGI
GENERATE PAGE DISPLAYING MEASUREMENT RESULTS AT SERVER
TRANSFER PAGE DISPLAYING RESULTS TO USER'S PC OVER THE INTERNET AND DISPLAY

FIG. 2.

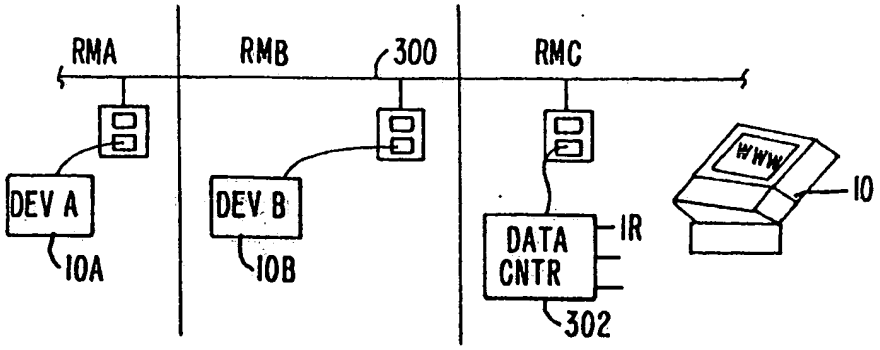
RMA
RMB
300
RMC
DEV A
10A
DEV B
10B
DATA CNTR
IR
302
WWW
10

FIG. 3.

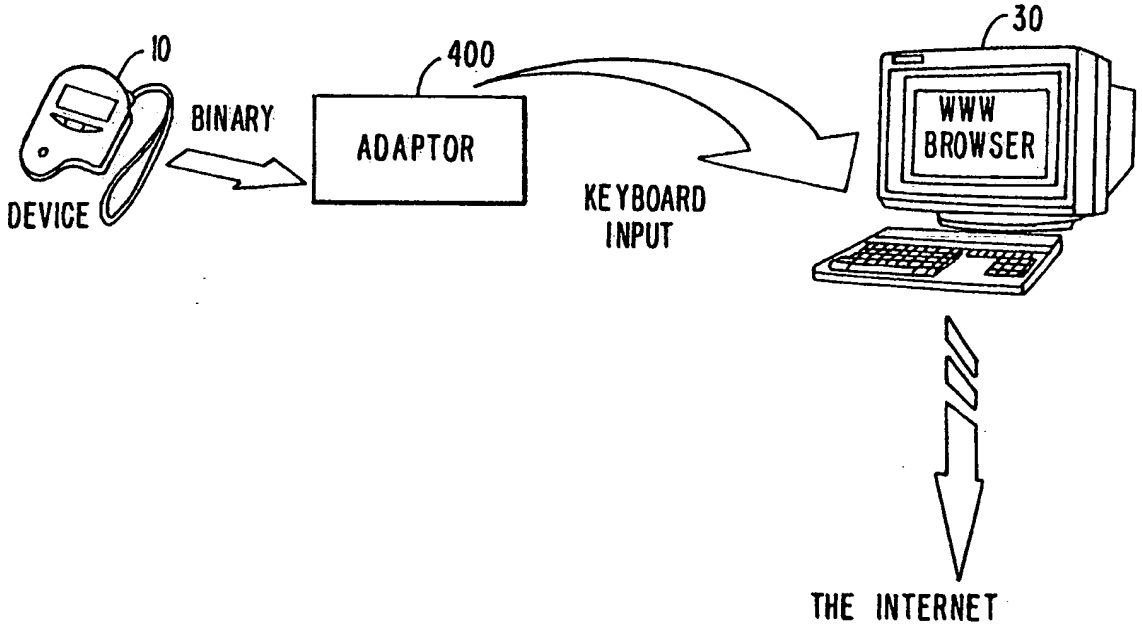
10
DEVICE
BINARY
400
ADAPTOR
KEYBOARD INPUT
30
WWW BROWSER
THE INTERNET

FIG. 4A.

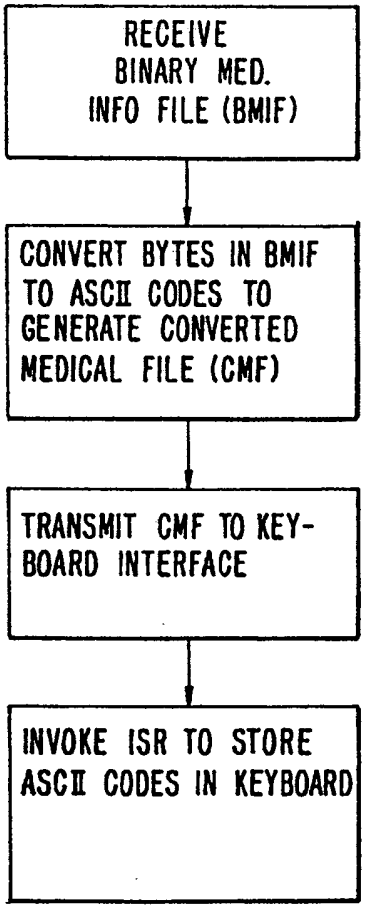
RECEIVE BINARY MED. INFO FILE (BMIF)
CONVERT BYTES IN BMIF TO ASCII CODES TO GENERATE CONVERTED MEDICAL FILE (CMF)
TRANSMIT CMF TO KEY-BOARD INTERFACE
INVOKE ISR TO STORE ASCII CODES IN KEYBOARD

FIG. 4B.

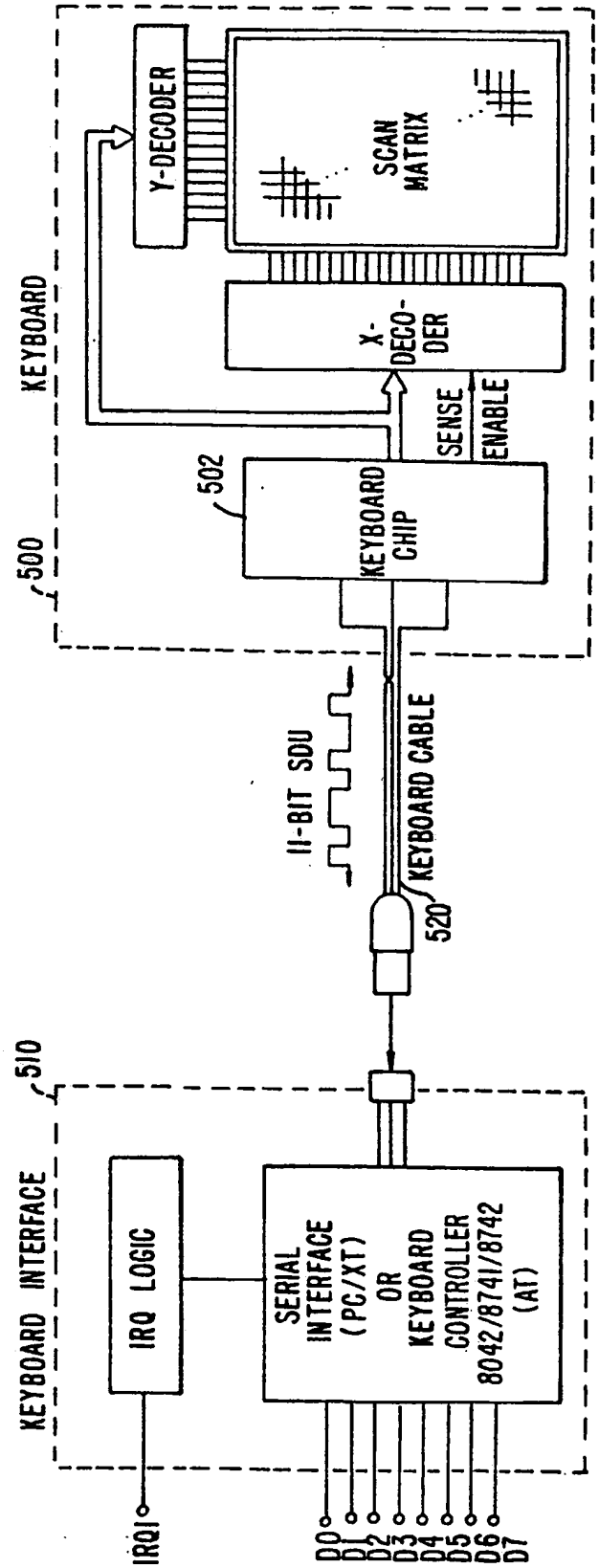

FIG. 5. PRIOR ART

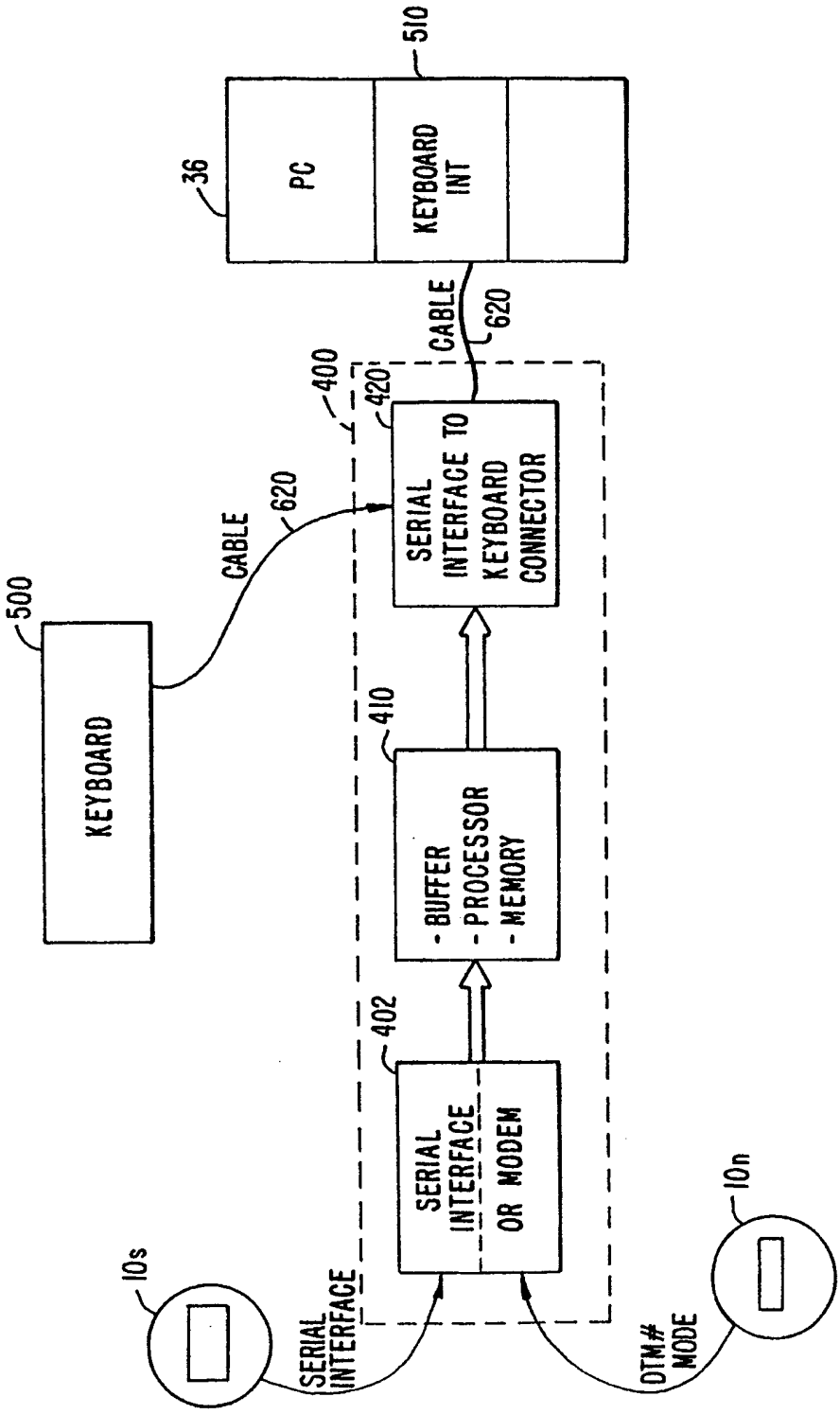
510
36
PC
KEYBOARD INT
CABLE
620
400
420
SERIAL INTERFACE TO KEYBOARD CONNECTOR
620
CABLE
500
KEYBOARD
410
- BUFFER
- PROCESSOR
- MEMORY
402
SERIAL INTERFACE OR MODEM
10s
SERIAL INTERFACE
10n
DTM# MODE

FIG. 6A.

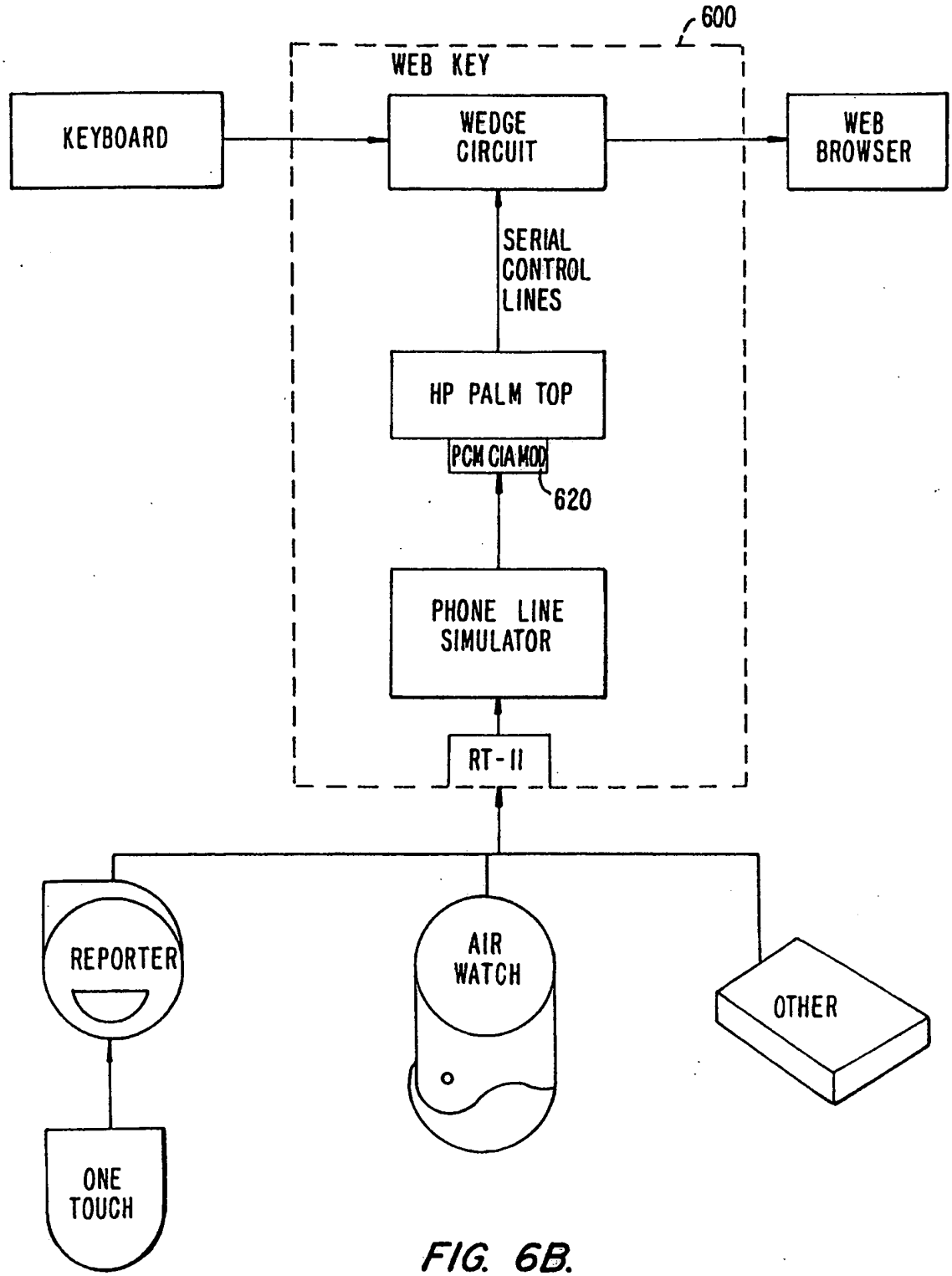
600
WEB KEY
KEYBOARD
WEDGE CIRCUIT
WEB BROWSER
SERIAL CONTROL LINES
HP PALM TOP
PCM CIA MOD
620
PHONE LINE SIMULATOR
RT-11
REPORTER
AIR WATCH
OTHER
ONE TOUCH

FIG. 6B.

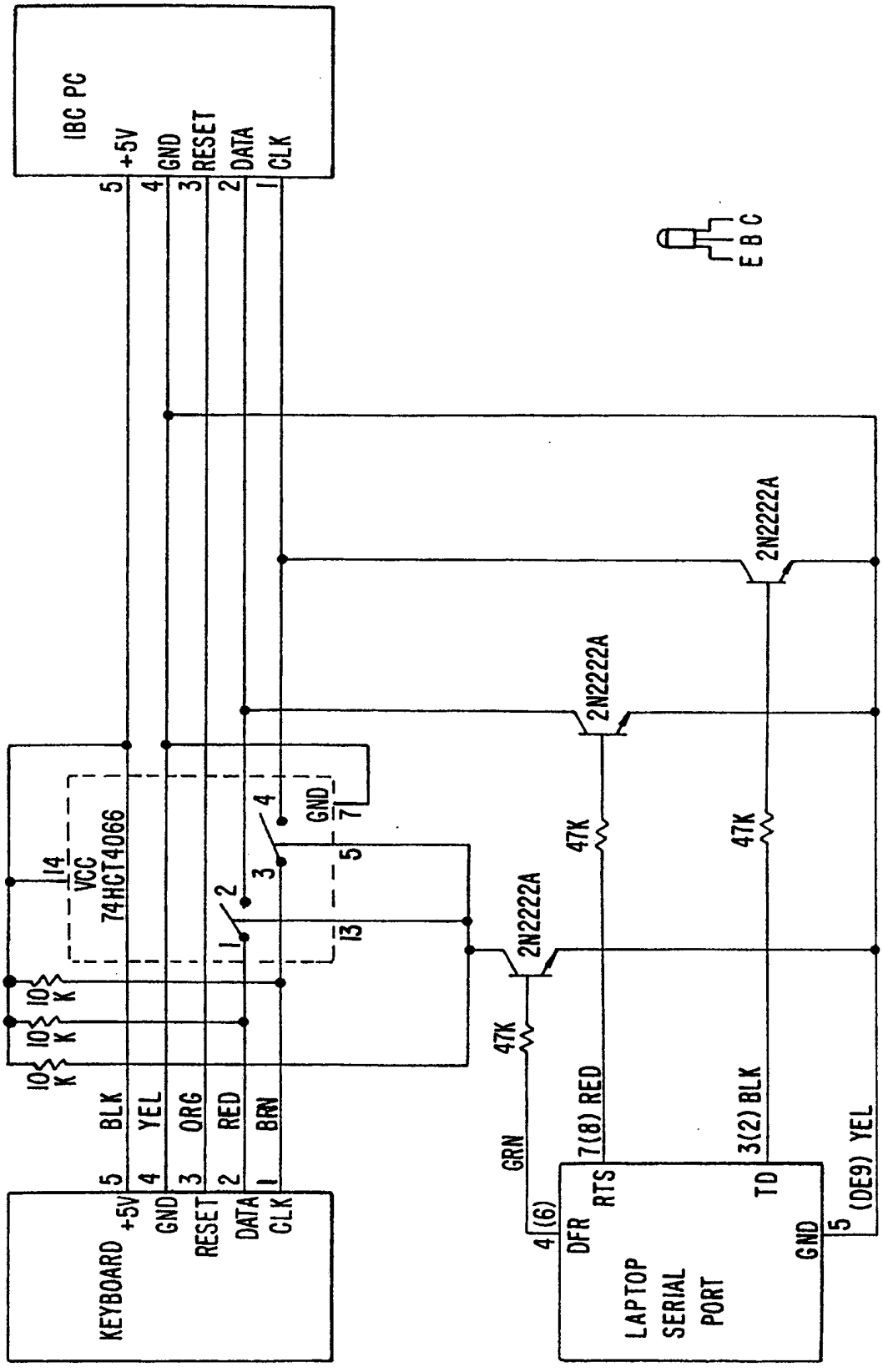
IBC PC
5 +5V
4 GND
3 RESET
2 DATA
1 CLK
E B C
2N2222A
2N2222A
2N2222A
47K
47K
47K
14
VCC
74HCT4066
13
GND
7
10 K
10 K
10 K
5 BLK
4 YEL
3 ORG
2 RED
1 BRN
KEYBOARD
+5V
GND
RESET
DATA
CLK
GRN
4 (6)
DFR
7(8) RED
RTS
3(2) BLK
TD
5 (DE9) YEL
GND
LAPTOP
SERIAL
PORT
( ) INDICATES NULL MODEM PINOUT

FIG. 6C.

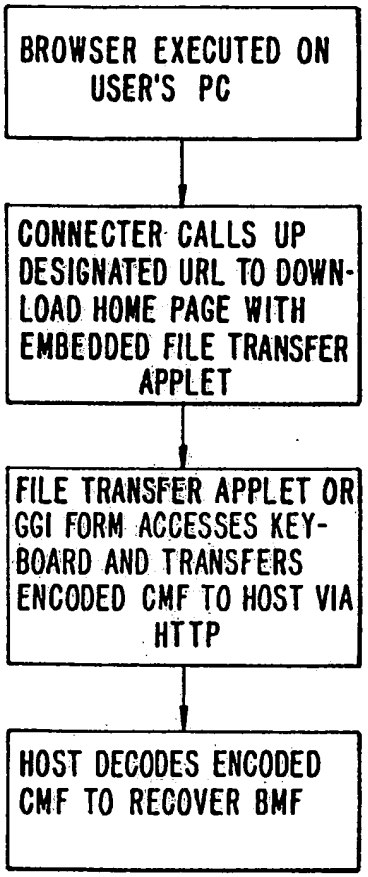
BROWSER EXECUTED ON USER'S PC
CONNECTER CALLS UP DESIGNATED URL TO DOWN-LOAD HOME PAGE WITH EMBEDDED FILE TRANSFER APPLET
FILE TRANSFER APPLET OR GGI FORM ACCESSES KEY-BOARD AND TRANSFERS ENCODED CMF TO HOST VIA HTTP
HOST DECODES ENCODED CMF TO RECOVER BMF

FIG. 7.

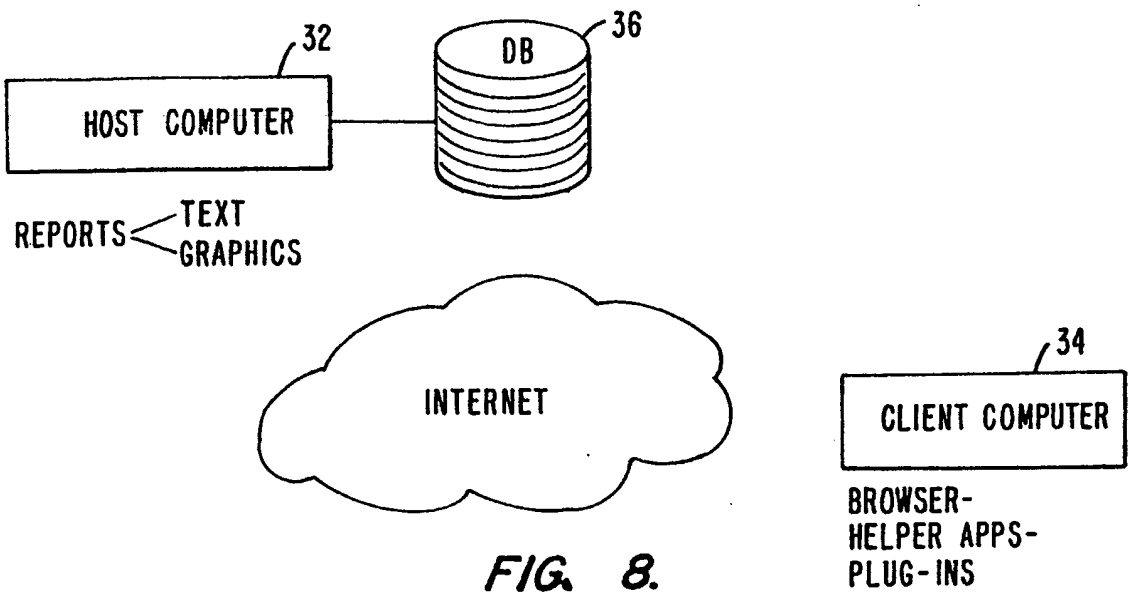
32
HOST COMPUTER
36
DB
REPORTS
TEXT
GRAPHICS
INTERNET
34
CLIENT COMPUTER
BROWSER-
HELPER APPS-
PLUG-INS

FIG. 8.

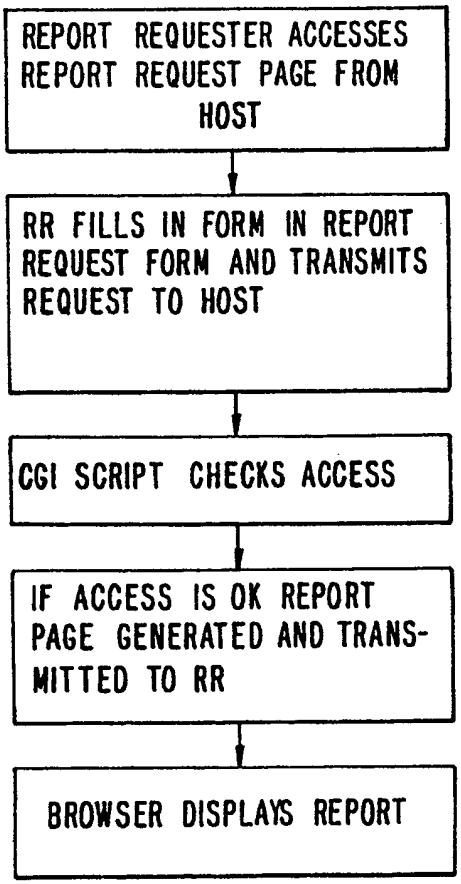
REPORT REQUESTER ACCESSES REPORT REQUEST PAGE FROM HOST
RR FILLS IN FORM IN REPORT REQUEST FORM AND TRANSMITS REQUEST TO HOST
CGI SCRIPT CHECKS ACCESS
IF ACCESS IS OK REPORT PAGE GENERATED AND TRANSMITTED TO RR
BROWSER DISPLAYS REPORT

FIG. 9.

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